

Epidemiologic features of cerebrovascular disease in Manitoba: incidence by age, sex and residence, with etiologic implications

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Summary: To determine the incidence of and risk factors in cerebrovascular disease in Manitoba, all 1367 new cases in defined areas (population, 660 391) in an 18-month period were studied. Pertinent data were collected from hospital records, death certificates and autopsy reports.

The annual incidence of cerebrovascular disease in these areas was 138/100 000 and the incidence was generally higher in men than in women. The incidence of cerebral infarction (INF) and that of hemorrhage (HGE) were similar in men and women less than 50 years old; thereafter the incidence of INF increased faster with age than did that of HGE, the disparity being greater in men than in women, whereas the incidence of HGE increased at similar rates in the two sexes. The incidence of INF was significantly greater in men than in women in urban areas, and in men it was greater in urban than in rural areas.

Elevated concentrations of serum lipids and smoking are implicated as risk factors in INF, and hypertension as a risk factor in HGE.

Résumé: Les caractéristiques épidémiologiques de l'accident vasculaire cérébral au Manitoba: l'incidence par âge, sexe et résidence, avec des implications étiologiques

En vue de déterminer l'incidence et les facteurs de risque des accidents cérébrovasculaires au Manitoba, la totalité des 1367 nouveaux cas survenus dans des régions bien définies (population, 660 391) durant une période de 18 mois a été étudiée. Les données pertinentes ont été recueillies dans les dossiers des hôpitaux, les certificats de décès et les rapports d'autopsies.

L'incidence annuelle de cette pathologie dans ces régions était de 138 par 100 000 personnes, cette incidence étant généralement plus élevée chez l'homme que chez la

femme. L'incidence de l'infarctus cérébral (INF) et celle de l'hémorragie (HGE) étaient similaires chez l'homme et chez la femme de moins de 50 ans. Passé cet âge l'incidence de l'INF augmentait plus vite avec l'âge que celle de l'HGE, la disparité étant plus grande chez l'homme que chez la femme, tandis que l'incidence de l'HGE augmentait au même rythme dans les deux sexes. Dans les régions urbaines l'incidence de l'INF était nettement plus grande chez l'homme que chez la femme. En outre, elle était plus élevée chez l'homme habitant des régions urbaines que chez celui qui habite des régions rurales.

Parmi les facteurs de risque de l'INF figurent une lipémie élevée et l'habitude de fumer. L'hypertension par contre est un facteur de risque pour l'HGE.

Cerebrovascular disease (CVD, "stroke") ranks third among the leading causes of death and is a major cause of disability in "developed" countries. However, compared with ischemic heart disease few studies have been carried out to determine the etiologic and risk factors of CVD. Lower incidence, older age at occurrence and the lack of simple, reliable diagnostic methods are among the major reasons population-based studies on stroke are rare. Many of the reports that have been published are based on mortality data from vital statistics records and on autopsy findings.

To avoid the high cost and difficulties of a cohort study in determining the incidence and risk factors of stroke, one can instead review the records of a large population defined by administrative boundaries when certain uniform conditions prevail, such as comprehensive medical care coverage administered by one authority for that population. In Manitoba medical care is provided for almost every resident virtually free, and the program is administered by the governmental Manitoba Health Services Commission (MHSC). Therefore, all new patients with a stroke admitted to hospitals in Manitoba during a specified period can be identified from the MHSC records and studied.

In this paper we present our findings on the incidence of stroke in Manitoba according to certain personal characteristics and residence, and attempt to explain these findings in terms of possible risk factors.

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Study design and methods

The MHSC was asked to provide hospital claim reports for patients with the diagnosis of CVD (ICD¹ rubrics 430 to 438) who were admitted to hospitals in Manitoba during the 18-month period Jan. 1, 1970 to June 30, 1971. For this study we included only patients admitted to hospitals in the greater Winnipeg area (Census Division 20), four other major census divisions in the south (1, 2, 5 and 9) and two large southern cities (Portage la Prairie and Brandon) because the majority of the population of Manitoba is concentrated in the south of the province, with approximately 50% in greater Winnipeg. The minority who live in northern Manitoba are scattered over a large area and their health care is provided by many small centres located far apart. However, for comparison, a few areas in the north (Flin Flon, Swan River, The Pas, Dauphin and Thompson) with a relatively large population have also been studied and the results will be analysed separately.

When all possible cases were identified from the MHSC claim reports, a field team of three research assistants (trained nurses) visited the hospitals in the areas under study and reviewed thoroughly the medical records of the patients. All relevant information was transferred to a special worksheet; included were details of personal characteristics, admission and discharge dates, personal and family histories of hypertension and cardiovascular disease, personal histories of diabetes and other diseases, and results of physical examination and laboratory investigation (chest radiography, electrocardiography and measurement of serum cholesterol and triglycerides, blood sugar, hemoglobin and hematocrit). When available, data from death certificates and reports on angiography, lumbar puncture and autopsy were also secured.

All worksheets were scrutinized by one of us (H.A.H.A.). The criteria for classification and diagnosis of CVD laid down by the ad hoc committee established by the advisory council for the National Institute of Neurological Disease and Stroke² were strictly followed to establish a diagnosis for every case. When sufficient evidence was available the case was assigned to one of two diagnostic categories: (a) cerebral infarction (INF), due to thrombosis, embolism or an unidentified cause; or (b) hemorrhage (HGE), of subarachnoid (SAH), intracerebral (ICH) or undetermined type. When sufficient evidence was not available to diagnose the type of stroke, the case was designated as "stroke of undetermined type". Patients who clearly had not had an acute stroke (e.g., arteriosclerosis without acute sustained neurologic manifestations, or transient ischemic attacks [TIA]) and patients with a history of a previous stroke were excluded, as were all patients who were not residents of Manitoba. Thus, of 3717 possible cases of CVD, 2233 were rejected because they failed to satisfy the criteria of a first acute stroke in a Manitoba resident.

Table 1—Distribution of cases of stroke by patient age and diagnostic category; Manitoba,* Jan. 1, 1970 to June 30, 1971

Age group (yr)	Type of stroke							
					Undetermined type		All types	
	Infarction		Hemorrhage					
	No.	%	No.	%	No.	%	No.	%
20 - 29	3	0.3	2	0.8	0	0	5	0.4
30 - 39	9	1.0	12	4.9	3	1.3	24	1.8
40 - 49	29	3.3	28	11.3	5	2.2	62	4.5
50 - 59	101	11.3	54	21.9	6	2.6	161	11.8
60 - 69	208	23.4	43	17.4	31	13.5	282	20.6
70 - 79	282	31.7	53	21.5	76	33.0	411	30.1
80 +	258	29.0	55	22.3	109	47.4	422	30.9
All ages	890	65.1	247	18.1	230	16.8	1367	100

*Greater Winnipeg area, four major census divisions and two cities in the south.

Among the 1484 remaining cases 1367 patients were from the southern part of the province, and this paper is based on analysis of their cases. Study of the other 117, from the northern part of the province, forms the basis of a separate report.

For adjusted rates we used the chi-square test described by Gart³ for testing the significance of the difference between proportions over a series of 2 x 2 tables (according to age); for testing the difference between separate age-specific rates we used the simple chi-square test.

Results

The 1367 new cases of stroke in this study occurred in a population of 660 391, for an overall annual incidence of 138/100 000. Of the total, 65.1% were INF cases (55.6% due to cerebral thrombosis, 9.2% due to embolism and 0.3% due to other causes) and 18.1% were HGE cases (5.6% SAH, 11.9% ICH and 0.6% other types of hemorrhage). The type of stroke could not be determined in 16.8% of cases. In the analysis to follow, comparisons were carried out between the two main groups, INF and HGE, since further subclassification by type would yield too few cases in each subgroup for reliable statistical results.

Distribution of the cases by patient age and diagnostic category is shown in Table I. A higher percentage of HGE than INF cases is seen in every age group below 60 years, and the reverse is observed in older groups. This pattern is apparent in both men and women (Fig. 1) and indicates that, in general, patients with HGE are younger than those

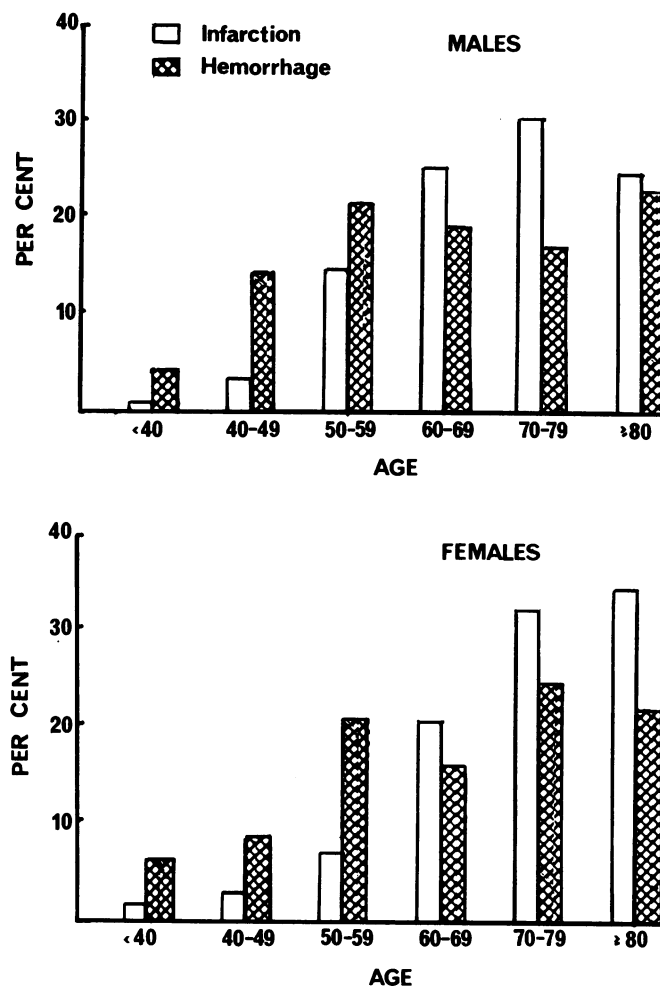


FIG. 1—Age distribution of 1137 patients with cerebral infarction or hemorrhage, by sex; Manitoba, Jan. 1, 1970 to June 30, 1971.

with INF. Also, the percentage of cases consistently increases with age in each diagnostic category except among the INF patients aged 80 or more and the HGE patients aged 60 to 69 (Table I). In men the percentage of INF cases increases with age up to 80 years and then decreases,

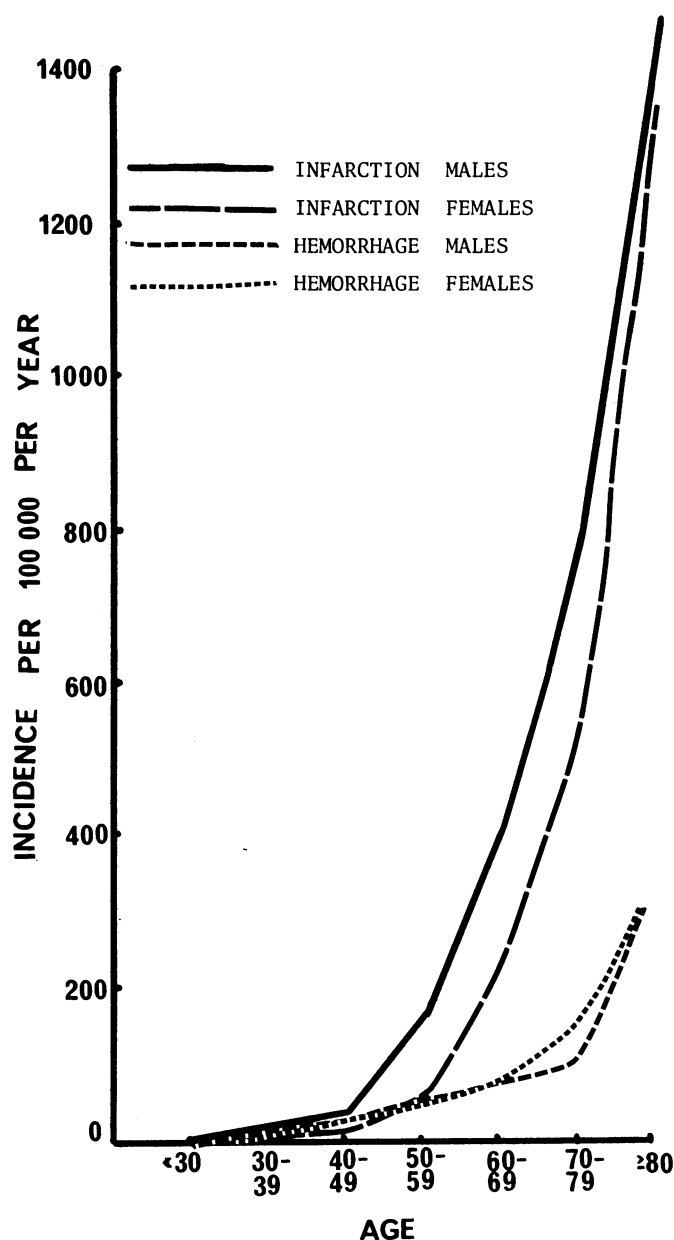


FIG. 2—Incidence of stroke, by diagnostic category, age and sex.

Table II—Annual incidence of stroke, by age and sex

Age group (yr)	Men			Women			Total		
	Population	No. of cases*	Rate†	Population	No. of cases*	Rate†	Population	No. of cases*	Rate†
< 30	174 953	2	1	172 608	3	1	347 561	5	1
30 - 39	39 347	10	17	40 150	14	23	79 497	24	20
40 - 49	39 122	38	65	42 047	24	38	81 169	62	51
50 - 59	32 141	102	213	33 981	59	116	66 122	161	163
60 - 69	20 961	167	534	23 157	115	333	44 118	282	426
70 - 79	13 708	213	1041	16 126	198	972	29 834	411	923
80 +	5 413	204	2525	6 677	218	2187	12 090	422	2339
All ages	325 645	736	151	334 746	631	126	660 391	1367	138
Age-adjusted rate			160.8			125.7			

*Number of cases in the 18-month study period.

†Rate per 100 000 per year.

but in women the percentage increases gradually and consistently with age. The percentage of HGE cases increases in both sexes with age up to 59 years and then decreases; after the age of 69 there are irregular differences between the sexes. However, the incidence of HGE in women is distinctly higher in those aged 70 to 79. As expected, the percentage of strokes of undetermined type increases steadily with age, particularly after the age of 60, reaching a maximum of 47.4% in the 80s (Table I); this indicates the difficulty in making a diagnosis in older patients.

The age-specific annual incidence rates of stroke, by sex, are shown in Table II. The age-adjusted rate of 160.8/100 000 in men is significantly higher than the rate of 125.7/100 000 in women ($P < 0.0005$). (The age distribution of the total population was used as a standard in adjusting for age.) Furthermore, all age-specific incidence rates for people more than 40 years old are higher in men than in women, with significant differences in the age groups 50 to 59 years ($P < 0.001$) and 60 to 69 years ($P < 0.008$); the incidence in people less than 40 years old is similar in the two sexes. The incidence of stroke increases steadily with age in each sex, but more rapidly in men.

The incidence of stroke, by diagnostic category, age and sex is shown in Fig. 2. The incidence of HGE is equal in men and women in each age group except 70 to 79, in which the rate is higher in women; however, this difference is not significant. The incidence of INF, on the other hand, is higher in men than in women, as indicated by the overall age-adjusted rates of 108.4 and 73.9/100 000 for men and women, respectively ($P < 0.0005$); by the age-specific rates of 403 and 237/100 000 for men and women, respectively, aged 50 to 59 ($P < 0.002$); and by the age-specific rates of 743 and 540/100 000 for men and women, respectively, aged 70 to 79 ($P = 0.026$). Below the age of 50 there is no significant difference in incidence of INF between men and women, and INF and HGE occur then at similar rates in men. After the age of 50 the incidence of INF increases much faster with age than that of HGE in men, whereas in women the rates of INF and HGE remain similar until the age of 60, after which the rate of INF increases faster than that of HGE.

Differences in the incidence of stroke by residence are also apparent in our data. Residence was classified into urban and rural according to whether a patient lived in the greater Winnipeg area (urban) or outside Winnipeg (rural). The age-adjusted incidence of stroke in rural areas was 134.3/100 000 and in urban areas, 139.5/100 000. This difference is not significant. However, possibly because of the expected lower diagnostic standards and facilities in rural areas, the incidence of undetermined types of stroke was higher in these areas than in urban areas for both men and women (age-adjusted rates: rural, 42.4 and 29.9; urban, 24.5 and 16.3, respectively). As the rates indicate,

the incidence of undetermined types was higher in men than in women in both areas.

In general, the higher overall incidence of stroke in men than in women is also seen within both urban (age-adjusted rates, 166.8 v. 117.6; $P < 0.0005$) and rural (age-adjusted rates, 143.7 v. 125.3; not significant) areas. Detailed analysis by diagnostic categories revealed that the incidence of INF in urban areas was higher in men than in women (age-adjusted rates, 117.6 v. 72.1; $P < 0.0005$). The age-specific incidence curves also show these differences, particularly after the age of 50 (Fig. 3).

In addition, the incidence of INF among men in urban areas was higher than that among men in rural areas (age-adjusted rates, 117.6 v. 80.3; $P < 0.0005$). The age-specific incidence curves of INF in men show the same pattern up to the age of 79; at age 80 and older the incidence is higher in rural areas (Fig. 4).

On the other hand, there are no significant differences in the incidence of INF between men and women in rural areas (age-adjusted rates, 80.3 v. 78.8), or in the incidence of all strokes or INF between women in urban as compared with rural areas (117.6 v. 125.3 and 72.1 v. 78.8, respectively). The age-specific incidence curves reflecting these patterns of INF are shown in Figs. 3 and 4, respectively.

As to HGE, the incidence was consistently higher in urban than in rural areas, as shown by the adjusted rates in men (24.7 v. 21.0; not significant) and in women (29.2 v. 16.6; $P < 0.05$). In addition, the incidence was higher in women than in men in urban areas (29.2 v. 24.7), whereas it was higher in men than in women in rural areas (21.0 v. 16.6); however, these differences are not significant. The age-specific incidence curves of HGE reflecting these differences are shown in Figs. 5 and 6. Higher rates of HGE are seen in urban than in rural areas among both men and women until the age of 80; the rural rates are higher thereafter. The incidence of INF and HGE was consistently higher in each sex in rural areas than in urban areas from the age of 80 on.

Discussion

The annual CVD incidence of 138/100 000 estimated in this report is low compared with rates reported for other parts of North America (Table III). There is no reason, however, to doubt the reliability and validity of this finding, for all cases were scrutinized, and, because the comprehensive, free hospital and medical care system in Manitoba ensures the admission of virtually all patients with a stroke to hospital, all subjects were, therefore, readily

identifiable. In only one study, conducted in the Jerusalem district,⁴ was the incidence of stroke lower than in our study (90/100 000); however, this study covered a relatively large community and a procedure similar to ours was followed for ascertainment of cases. The reported differences in incidence of stroke between these studies may be due to differences in diagnostic criteria, population distribution by age and sex, and other factors.

When the incidence rates of stroke by diagnostic category in these studies are compared, the Manitoba rates are intermediate except for that of SAH, which is the lowest but not much different from some others. The Framingham Study^{9,10} reported the highest rates of cerebral embolism and SAH, a pattern that is also apparent in the distribution of stroke by type (Table IV) and probably reflects the fact that the subjects were selectively younger (30 to 60 years

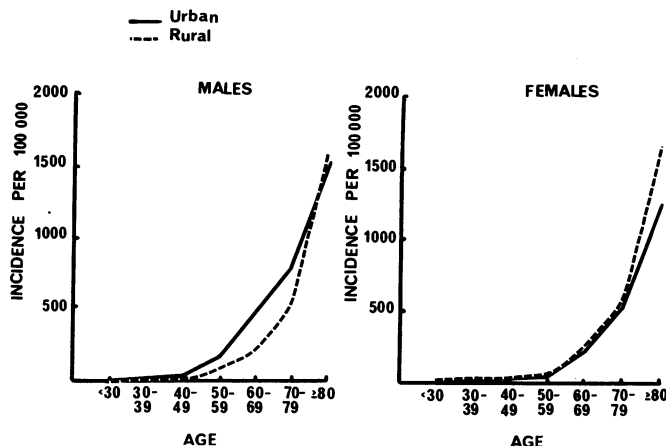


FIG. 4—Age-specific incidence of infarction, by residence, in men and women.

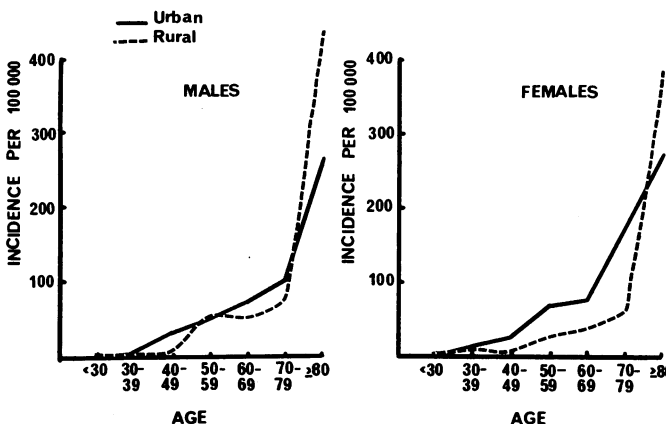


FIG. 5—Age-specific incidence of hemorrhage, by residence, in men and women.

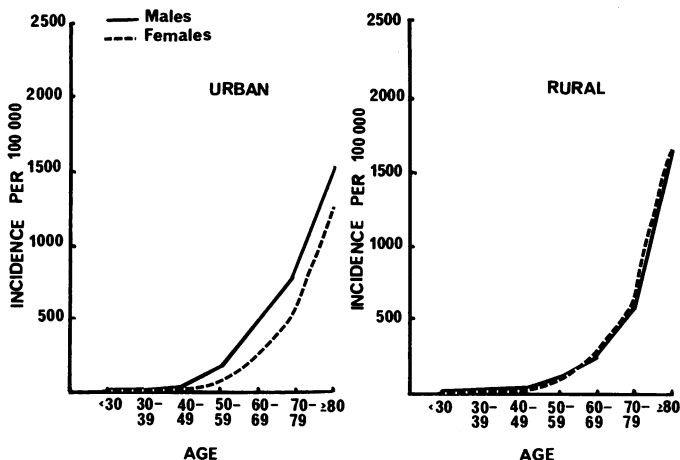


FIG. 3—Age-specific incidence of infarction, by sex, in urban and rural areas.

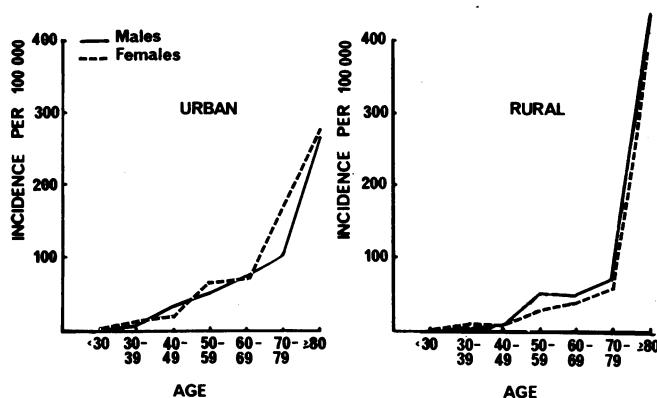


FIG. 6—Age-specific incidence of hemorrhage, by sex, in urban and rural areas.

old); indeed, the proportions of embolism and SAH cases in the 16-year follow-up report¹⁰ were less than those in the earlier 12-year follow-up report,⁹ which probably reflects the ageing of the population. Manitoba is again in an intermediate position when distribution by type of stroke is compared. Despite the differences between these studies, in all, cerebral thrombosis accounts for the largest proportion of stroke cases, followed by cerebral hemorrhage (in most studies), then embolism and SAH (except in the Framingham Study).

The incidence rates of stroke by sex and age in this

study provide conclusive evidence that this disease generally occurs more often in men than in women, particularly in people more than 50 years old. This difference is mainly attributed to the incidence of INF. Before the age of 50 there is no sex difference in the incidence of all strokes or of specific types.

Some earlier studies found no sex difference in the incidence of stroke,^{5,8,9,12} but more recent ones, including the community study in Jerusalem,⁴ the recent extension of the Rochester study,⁶ a United States nationwide study by Kuller and colleagues¹¹ and a prospective study in Japan,¹³

Table III—Annual incidence* of stroke, by type, in various studies

Reference no.	Place	Population	No. of cases	Cerebral thrombosis		Cerebral embolism		Cerebral hemorrhage		Subarachnoid hemorrhage		Other strokes		Total strokes	
				No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate
Present study	Manitoba	660 391	1367	760	77	126	13	162	16	77	8	242	25	1367	138
4	Jerusalem district 1960-67	208 750	1522	509	30†	—	—	181	11‡	—	—	832	49	1522	90
5	Rochester, Minnesota 1945-54	28 247	548	412	146	16	6	53	19	30	11	37	13	548	194
6	Rochester, Minnesota 1955-69	42 809	993	701	109	76	12	100	16	63	10	53	8	993	154§
7	Rochester, Minnesota 1957	35 000	64	32	80†	—	—	10	24	6	16	16	40	64	170
8	Middlesex, Connecticut¶	83 500	191	91	110 (80)	4	5	68	80‡ (60)	—	—	28	30 (30)	191	230 (170)
9	Framingham, Massachusetts	5 106	90	57	93	13	21	4	7	16	26	—	—	90	165
10	Framingham, Massachusetts	5 106	153	93	114	22	27	10	12	20	24	8	10	153	187

*All rates are annual rates per 100 000 population.

†Including embolism.

‡Including subarachnoid hemorrhage.

§The rate for the period 1965-69 was 141.

¶Rates in parentheses were adjusted according to the age distribution of the population of the United States.

Table IV—Percent distribution by type of stroke in various studies

Reference no.	Place	Total no. of cases	Percent of total cases				
			Thrombosis	Embolism	Cerebral hemorrhage	Subarachnoid hemorrhage	Unidentified types
Present study	Manitoba	1367	55.6	9.2	11.9	5.6	17.7
8	One county, Connecticut	191	48	2	36*	—	14
4	Jerusalem district	1522	33†	—	12*	—	55
5	Rochester, Minnesota	548	75.2	2.9	9.7	5.4	6.8
6	Rochester, Minnesota	993	70.6	7.7	10.1	6.3	5.3
9	Framingham, Massachusetts	90	63	15	4	18	—
10	Framingham, Massachusetts	153	60.8	14.4	6.5	13.1	5.2
11	Eight areas in United States	2619‡	43.5	5.4	17.4	8.5	25.2

*Includes subarachnoid hemorrhage.

†Includes embolism.

‡76% had no past history of stroke, or the history was unknown.

reported findings similar to ours — namely, that stroke occurs more often in men than in women. Two of these studies^{4,6} show patterns by age, sex and diagnostic category similar to ours. These patterns should not be overlooked, for they may lead to clues to the risk factors in stroke. Further clues may be found if other differences, by for example geographic locale, are detected.

In further support of the sex difference in the incidence of stroke is the consistent finding both in rural and in urban areas that strokes occurred more often in men than in women. However, when diagnostic categories were considered individually, it was found that the incidence of INF alone was significantly higher in men than in women in urban areas only; and in men, it was higher in urban than in rural areas. From this it appears that living in urban areas somehow predisposes men to INF.

The lack of significant differences in the incidence of INF between men and women in rural areas, as well as between women in rural and urban areas, should be viewed cautiously, for the incidence of undetermined types of stroke is higher in rural than in urban areas and is also higher in men than in women. If a large proportion of the undetermined types of stroke in men in rural areas turned out to be INF cases, a similar significantly higher rate of INF in men than in women in rural areas would probably have emerged. In this case the factor (or factors) predisposing to INF would probably be a basic difference between men and women in general, regardless of residence. It is difficult to speculate on the undetermined cases, but our planned comparison of control subjects in different age, sex and residence categories, and between patients and controls, with respect to possible risk factors, will undoubtedly clarify the situation.

At this point we can speculate on the possible risk factors that may fit the observed patterns of incidence of INF by sex, age and residence in this study. Atherosclerosis (caused by high concentrations of serum lipids and possibly other unknown factors) occurs more commonly in men than in women and it increases in frequency and severity with age, probably more rapidly in men than in women. Atherosclerosis may be more frequent and more severe in men in urban areas compared with men in rural areas, but this has yet to be determined. Cigarette smoking is more frequent and heavier among men than among women. It may also be that men in urban areas smoke more heavily than those in rural areas.

Despite the fact that elevated concentrations of serum lipids (particularly cholesterol) have been indicated as a definite risk factor in coronary heart disease, findings on their importance in stroke conflict. Some case-control studies¹⁴⁻¹⁶ and the Framingham Study^{9,10} support the association of elevated serum lipid values with stroke, whereas others refute this association.^{12,17-19} This disagreement in findings may be due to the failure to consider individual diagnostic categories of stroke separately in evaluating the risk, to selective studying of specific age groups, or to small sample sizes. We believe serum lipids may be an important factor in INF, as suggested from our findings and from those of other studies, as well as from the reported association of diabetes — in which atherosclerosis is common — with INF but not with HGE.²⁰

Since both INF and HGE occur infrequently and at

more or less equal rates in men and women less than age 50, regardless of residence, it seems that there is no differential role of the risk factors in each type before that age. At older ages high blood pressure may be an important factor in the occurrence of HGE; in this study the incidence of HGE was generally similar in men and women, with a slight preponderance in women, and this pattern may parallel the differential distribution of blood pressure between men and women. The higher blood pressure and higher incidence of HGE in blacks compared with whites^{21,22} supports this theory. However, neither blood pressure nor serum lipids is believed to be an exclusive risk factor for HGE and INF, respectively; rather, both are probably important in most strokes, but to a different degree, depending on the type of stroke.

This discussion is mere speculation, in which we have tried to relate the observed incidence of stroke in this study to possible risk factors. It is in no way conclusive but, considered with the findings in other studies, may support or generate certain hypotheses.

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